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The characteristics of patients undergoing endobronchial ultrasonography-guided transbronchial needle aspiration (EBUS-TBNA): single-center experience

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ABSTRACT

Aims: We aimed to present the features of our Endobronchial ultrasonography-guided transbronchial needle aspiration (EBUS-TBNA) cases, the lymph nodes that were biopsied, their pathological diagnoses, and the complications that developed due to the procedure.

Methods: All cases who underwent EBUS-TBNA between January 2016 and December 2023 in the chest diseases clinic of a training and research hospital were retrospectively screened. The patients who underwent the procedure (n=274) were included in the study. Cases in which fine needle aspiration biopsy was performed with EBUS-TBNA and the material obtained was not diagnostic (n=3) or in which the pathology result could not be obtained in the files (n=9) were excluded from the study. The design of our study was cross-sectional and planned as a descriptive study.

Results: Of the 262 patients included in the analysis, 66.4% (n=174) were male and the average age of the population was 60.8±11.4 years. When EBUS-TBNA indications were evaluated, the procedure was performed for diagnostic purposes in 96.9% (n=254) and for re-evaluation after chemotherapy in 3.1%. EBUS-TBNA procedure was performed in 16.8% (n=44) patients due to mediastinal mass and in 83.2% (n=218) patients due to mediastinal lymphadenopathy. The most common stations where biopsy is performed with the EBUS-TBNA process are the subcarinal (7) and lower right paratracheal (4R) lymph node stations. When the biopsy results were evaluated, malignancy was reported in 54.6% (n=143) of the patients. The complications related to the EBUS-TBNA procedure were generally mild and trancient .

Conclusion: EBUS-TBNA is a minimally invasive method used in the diagnosis and staging of lung cancer, the evaluation of non-endobronchial lesions, the diagnosis of benign diseases of the mediastinum, and the diagnosis of mediastinal metastases of extrathoracic malignancies. In experienced centers like our clinic, the diagnostic value of the procedure is high and the complication rates are very low.

Keywords: EBUS, lung cancer, metastasis

INTRODUCTION

Endobronchial ultrasonography-guided transbronchial needle aspiration (EBUS-TBNA) plays an important role in the diagnosis and staging of lung cancer, mediastinal restaging after lung cancer treatment, evaluation of possible mediastinal lymph node metastases of extrathoracic primary cancers, diagnosis of lymphoma, infectious and granulomatous diseases, and determination of nodal localizations.[1-3] In addition, in recent years, cytopathological sampling for genotyping and immunohistochemical analysis in targeted therapies in lung cancer has been recommended many guidelines as the first choice diagnostic tool.[4]

EBUS-TBNA is a minimally invasive procedure that enables direct bronchoscope imaging and sampling of mediastinal and hilar lymph nodes and masses adjacent to the trachea and bronchi, and provides equivalent diagnostic accuracy and reliable patient safety when compared to traditional invasive techniques such as mediastinoscopy and thoracoscopy.[5]

When EBUS-TBNA is performed by experienced physicians, its diagnostic value is high and procedure complications are observed less frequently. In addition, the recovery time to return daily life after the procedure is much shorter than surgical procedures, and the loss of labor per working days is significantly shorter. The EBUS-TBNA process is reproducible, does not cause any permanent anatomical changes, and is advantageous compared to surgical biopsies. Some of these advantages include the absence of many factors that reduce

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the quality of life, such as wound healing after the procedure, dressing requirements, surgical site infections, and post-surgical pain.

We have been performing EBUS-TBNA procedures for approximately 8 years by experienced chest diseases specialists in our center, which started in a chest diseases branch hospital and grew as a training and research hospital. We aimed to present the features of our EBUS-TBNA cases, which we thought would contribute to national data, the lymph nodes that were biopsied, pathological diagnoses, and complications related to the procedure.

METHODS

This study was carried out with the approval of the Samsun University Clinical Researches Ethics Committee (Date: 18,10,2023, Decision No: 2023/19/2). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

All cases who underwent EBUS-TBNA at the Chest Diseases Clinic of Samsun Training and Research Hospital between January 2016 and December 2023 were retrospectively screened . The patients who underwent the procedure (n=274) were included in the study. Cases in which fine needle aspiration biopsy was performed with EBUS-TBNA and the obtained material was not diagnostic (n=3) or in which the pathology result could not be reached in the records (n=9) were excluded from the study (Figure). The design of our study is descriptive study.

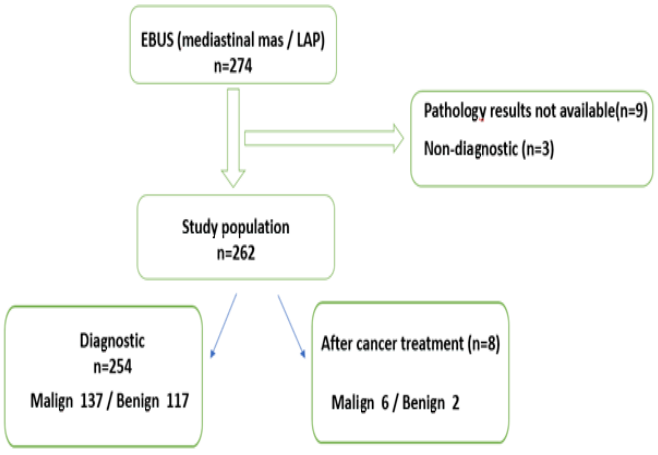

Figure. Patient's flowchart

The data were evaluated and, the main EBUS-TBNA indication was the presence of mediastinal lymphadenopathy or mass lesion on computed thorax tomography. The second indication was incidentally found lesions on PET-CT performed for screening purposes. The cases in which the short axis of any lymph node was larger than 1 cm and/or any involvement at the level of malignancy (SUVmax≥2.5) were evaluated by EBUS-TBNA.

The written informed consent forms were obtained from all patients before the EBUS-TBNA procedure. The EBUS-TBNA procedure was performed orally in the operating room under sedation with propofol, in a supine position with spontaneous breathing.

EBUS-TBNA is performed using thorax computed tomography or PET-CT, where the short axis is greater than 1 cm and/or involvement at the level of malignancy is reported on PET-CT, or the short axis is not reported on CT and PET-CT but detected by EBUS over 0.5 cm. At least two biopsies were taken from each focus on lymph node stations (4R, 4L, 7, 10R, 10L, 11R, 11L) and mediastinal masses using Fujifilm's EB-530US EBUS device and a 22-gauge disposable needle. Aspirates were spread on glass slides, air dried, and fixed with 95% alcohol. Histological aspirate tissues were fixed with 10% neutral buffered formalin for pathological examination. Rapid on-site evaluation (ROSE) was not performed during the procedure. In this study, demographic data of the patients, foci biopsied with EBUS-TBNA, pathological diagnoses and procedure-related complications were recorded.

Statistical Analysis

All data were analyzed with SPSS V 23 Windows statistical program (SPSS Inc., Chicago, IL, USA). Frequencies and percentage values of categorical variables; Mean and standard deviation values of numerical variables were calculated.

RESULTS

Of the 262 patients included in the analysis, 66.4% (n=174) were male and the mean age of the entire population was 60.8±11.4 years. When EBUS-TBNA indications were evaluated, the procedure was performed for diagnostic purposes in 96.9% (n=254) and for re-evaluation after chemotherapy in 3.1%. The average age of the cases was 60.8±11.4 years. The mean age of women in the population was lower than men (59.2±11.6 vs 61.5±11.3).

EBUS-TBNA procedure was performed in 16.8% (n=44) patients due to mediastinal mass and in 83.2% (n=218) patients due to mediastinal lymphadenopathy. The most common stations where biopsy is performed with the EBUS-TBNA process are the subcarinal (7) and lower right paratracheal (4R) lymph node stations (Table 1).

When the biopsy results were evaluated, malignancy was reported in 54.6% of the patients (n=143) (Figure). In patients with malignant pathology, the most common subtype was adenocarcinoma (n=50), followed by small cell carcinoma (n=31) and squamous cell carcinoma (n=24), respectively. The most common extrathoracic malignancy metastases were breast (n=5) and bladder (n=2) carcinoma. Among non-malignant findings, normal lymph node cytopathology (n=59) was most frequently reported. The most common benign pathology was sarcoidosis (n=41), followed by anthracosis (n=11) (Table 2).

Complications related to the EBUS-TBNA procedure were generally mild and trancient . Mild hemorrhage, which was controlled during the procedure, was observed in 10 (0.07%) patients. Short-term desaturation due to general anesthesia which was recovered with oxygen support, was observed in 12 (0.04%) patients. After the end of the procedure, no complications requiring treatment or hospitalization or prolonging hospital stay were observed.

Table 1. Demographic data of patients who underwent EBUS procedure	
Age; year (mean±SD)	60.8 ± 11.4
Gender	n (%)
Male	174 (66.4)
Female	88 (33.6)
Stations with EBUS	(%)
Lymph node	218 (83.2)
4 R	44 (16.8)
4 L	1 (0.4)
7	133 (50.8)
11 R	19 (7.3)
11 L	21 (8)
Mass	44 (16.8)
Procedure-related complications	n (%)
Hemorrhage (mild)	10 (0.07)
Desaturation	12(0.04)

R: Right, L: Left, SD: Standard deviation, EBUS: Endobronchial ultrasonography

Table 2. EBUS pathology diagnoses	
Pathology	**n (%)**
MALIGN	143 (54.6)
NSCLC	
Adenocarcinoma	50 (19.1)
Squamous cell carcinoma	24 (9.2)
Non-small cell carcinoma (type indistinguishable)	20 (7.6)
large cell carcinoma	1 (0.4)
SCLC	31 (11.8)
Lymphoma	6 (2.3)
Breast carcinoma metastasis	5 (1.9)
Bladder carcinoma metastasis	2 (0.8)
Cervix carcinoma metastasis	2 (0.8)
Renal cell carcinoma metastasis	1 (0.4)
Pleomorphic adenoma	1 (0.4)
BENING	119 (45.4)
Normal cytology	59 (22.5)
Sarcoidosis	41 (15.6)
Anthracosis	11 (4.2)
Tuberculosis	5 (1.9)
Pneumoconiosis	2 (0.8)
Invasive pulmonary aspergillosis	1 (0.4)

NSCLC: Non-small cell lung cancer, SCLC: Small cell lung cancer, EBUS: Endobronchial ultrasonography

DISCUSSION

Lung cancer is one of the leading causes of cancer-related deaths. According to WHO data, it is the most common cancer in men and the third most common in women, is often diagnosed in advanced stages, and is largely preventable because it is directly related to tobacco exposure.[6] In addition, the lungs and mediastinal lymph nodes are areas where extrathoracic malignancies frequently metastasize. Therefore, rapid diagnosis and accurate staging are very important in primary lung cancer or metastatic mass and lymph node metastases. Mediastinal lymph node involvement is the most important parameter to determine the type of treatment and staging before surgery, and deciding whether surgery will be recommended to the patient or not. EBUS-TBNA has a very important role in the diagnosis and staging of lung cancer. In the study by Torre et al. in which EBUS-TBNA results were evaluated including 456 cases, it was found that EBUS-TBNA had an accuracy rate of 97.1% in the diagnosis of primary lung cancer and 96.2% in the diagnosis of malignancy. In this study, the distribution of malignant diseases were 46.3% adenocarcinoma, 11.5% large cell, 10.4% squamous cell, and 10.7% small cell carcinoma.[7]

In Yılmaz et al.'s[8] study, EBUS-TBNA performed for mediastinal staging in 37 patients diagnosed with lung cancer and 37 patients for diagnostic purposes, sensitivity was found to be 83%, specificity was 100%, positive predictive value was 100%, negative predictive value was 70%, and accuracy was 88%. The diagnostic distribution of 37 cases biopsied with EBUS-TBNA was as follows: 19 cases were diagnosed with lung cancer, 5 cases with extra-thoracic cancer metastasis, 5 cases with sarcoidosis, 2 cases with tuberculosis, and 6 cases with benign lymph adenomegaly. The distribution of malignant diseases in our study population was as follows: 50 cases of adenocarcinoma, 31 cases of small cell carcinoma, 24 cases of squamous cell carcinoma, 20 cases of undifferentiated non-small cell carcinoma, and 1 case of large cell carcinoma. In our study, unlike other studies, EBUS-TBNA was also performed on masses adjacent to the trachea and bronchi.

The surgically treated lung cancer patients are followed-up radiologically for recurrence or second primary occurrence. Again, treatment response evaluation of lung cancer cases which are still under treatment is done by radiological methods. One of the most common clinical problems for clinicians in the follow-up of such patients is an emergence of a mediastinal lymph node whose diameter increase exceeds the limits or a lymph node with uptake slightly above the limit on control PET-CT. In these cases, especially those who have undergone thoracotomy or mediastinoscopy, repeated surgical biopsy is almost impossible due to postoperative adhesions, altered anatomy, and possible fibrosis after radiotherapy or surgery. In these cases, EBUS-TBNA provides significant advantages in both the ability to obtain reproducible biopsies and the ability to perform characteristic examination of the lymph node with ultrasonography. Additionally, another area where EBUS-TBNA is used is the restaging of lung cancer. In their study by Öztürk et al.,[9] in which they restaged patients who underwent chemoradiotherapy (n=26) and radical surgery (n=74), EBUS-TBNA had high diagnostic accuracy (93.2% after surgery, 100% after chemoradiotherapy). They reported that the sensitivity after surgery was 84.8% and, 100% after chemoradiotherapy. In our study, EBUS-TBNA

was performed on 8 patients who received treatment for lung cancer. Malignancy recurrence was reported in 6 patients, normal lymph node cytopathology was reported in 2 patients.

Apart from malignancies, EBUS-TBNA is frequently used in the detection of benign pathologies that cause mediastinal lymphadenopathy, especially in the diagnosis of granulomatous diseases such as tuberculosis and sarcoidosis.[9] In their study, Batum et al.[10] reported that EBUS-TBNA had a specificity of 86.6% and sensitivity of 98.3% in benign diseases, specificity of 100% and sensitivity of tuberculosis as 81.9%, and specificity of 100% and sensitivity of 95% in sarcoidosis. In their study, 590 patients were evaluated and the final diagnoses of the patients were reported as 62.7% non-granulomatous benign disease (n=370), 28.8% sarcoidosis (n=170), and 8.4% tuberculosis (n=50). In the study of Ortaköylü et al.[11] which data included from Turkey, the diagnostic distribution of the cases which reported benign disease was reported as 27% sarcoidosis and 8.8% tuberculosis. In our study, benign pathologies (n=119) were reported as sarcoidosis in 15.6%, anthracosis in 4.2%, and tuberculosis in 1.9%. Additionally, the pathological result was reported as normal lymph node cytopathology in 22.5% (n=59) of our cases. While the majority of these cases were followed up clinically and radiologically, some suspicious cases were referred to the thoracic surgery clinic for mediastinoscopy.

The role of EBUS-TBNA in the investigation of mediastinal lymph node metastases of extrapulmonary malignancies has not been widely studied. Mediastinal and hilar lesions are common findings on imaging in patients with extrathoracic primary cancers. Distant metastasis, disease recurrence and second primary malignancy can be diagnosed in a newly diagnosed patient. It may also indicate granulomatous disease in a previously diagnosed and treated patient. The role of EBUS-TBNA has previously been evaluated in several clinical studies, with reported sensitivity values (81-95%) and negative predictive values falling on a highly variable spectrum. While metastasis was detected in approximately 50% of these cases, a second primary malignancy, most commonly in the lung, was reported in 25%. Additionally, granulomatous inflammation such as tuberculosis and sarcoidosis was detected in a significant number of patients.3 As one of the largest studies published in our country, Demirdöğen et al.[12] evaluated the EBUS-TBNA results of a large number of patients with extrathoracic malignancies. Accordingly, it was reported that metastases were detected in 14.7% (n=16) of 109 patients with extrathoracic malignancy in EBUS-TBNA. In other studies, the most common extrathoracic malignancies were found to be head and neck malignancies, breast carcinomas, urological malignancies and gastrointestinal system tumors.[13-16] In our study, the most common disease with extrathoracic mediastinal metastasis was breast carcinoma, followed by urological malignancies.

Rapid pathological evaluation (ROSE) can be performed per case by a cytopathologist during the EBUS procedure. Although there is no difference in the final pathological diagnosis between cases in which ROSE was performed and those in which it was not performed, there are studies proving that it shortens the procedure time, reduces anesthesia-related complications, and allows adequate sample collection with fewer lymph node accesses.[17] Since there are not enough cytopathologists in our hospital, ROSE cannot be performed in EBUS-TBNA cases. Despite this, among our cases, the number of cases in which we reoperated due to insufficient cytopathological material was only.[3]

In the literature, most complications related to the EBUS-TBNA procedure are reported as case reports, and no deaths have been reported. In a meta-analysis in which 1299 patients were evaluated, the complication rate was reported as 0.15%,[18] and in another multicenter study in which 3123 patients were evaluated, the major complication rate was reported as 0.16%.[19] The most common complications include infection (mediastinitis, pneumonia or pericarditis), bleeding, pneumothorax, mediastinal emphysema and vocal cord damage. In our cases, complications related to the EBUS-TBNA procedure were generally mild and trancient. Mild hemorrhage, which was controlled during the procedure, was observed in 0.07% (n=10). During general anesthesia, short-term desaturation was observed due to sedation, which was recovered with oxygen support at a rate of 0.04% (n=12). After the end of the procedure, no complications requiring treatment or hospitalization or prolonging hospital stay were observed.

Limitations

The limitations of our study are that it is single-center and retrospective. Apart from this, follow-up results cannot be obtained because most of the malignant patients are followed up in oncological follow-up in another center from the moment of diagnosis.

CONCLUSION

EBUS-TBNA is a minimally invasive method used in the practice of the department of Chest Diseases in the diagnosis and staging of lung cancer, the diagnosis of non-endobronchial lesions, the diagnosis of benign diseases of the mediastinum and the diagnosis of mediastinal metastases of extrathoracic malignancies. In experienced centers like our clinic, the diagnostic value of the procedure results is high and the complication rates are very low.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Samsun University Clinical Researches Ethics Committee (Date: 18,10,2023, Decision No: 2023/19/2).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement
The authors have no conflicts of interest to declare.

Financial Disclosure
The authors declared that this study has received no financial support.

Author Contributions
All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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